

A beach head on an untamed
shore: a physician-ethicist
addresses living kidney donor
selection

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Living Donor Kidney Transplants

- Comprise 4,000 of 12,000 total transplants/year
- Provide 50% of kidney function initially.
- Living donor kidneys last 15 years; deceased donor kidneys last 9 years on the average.
- 100,000 patients begin dialysis each year.
- Waiting times lengthen each year (3-5 years).
- Centers teach, evaluate, and select donors.

What transplant centers do well

- Recognize the ethical complexity of their situation in selecting living kidney donors.
- Often make the right decisions in practice regarding donor motives.
- No consensus on the approach to donor long term medical risk (of kidney disease).

Transplant centers may or may not exclude kidney donors with common “isolated medical abnormalities.”

- Hypertension 54-64%
- Hematuria 31%
- Nephrolithiasis 34%
- Proteinuria 58%
- Low GFR 59%
- Diabetic risk 46-61%

(Bia et al, Transplantation 60:322-7, 1995; Mandelbrot et al, AJT, 2007)

Center response to kidney donors with isolated medical abnormalities.

- Try to resolve uncertainty by forums and papers in the specialty literature.
- “Up or down” voting on what donor medical findings are “acceptable.”
- No attempt to formulate and quantify risks.
- Use the “safe/unsafe” dichotomy

Doctor: "Mrs. Jones, your blood pressure is 140/90. It's too risky for you to donate a kidney."

Mrs. Jones: "All right, but what IS my risk?"

Doctor: "What do you mean?"

Mrs. Jones: " You say it's 'too risky,' so what IS the risk then, doctor, 1 in 10 or 1 in 100?"

Doctor: "I don't know how to answer that."

Mrs Jones: "Then I have to ask if you know what you're doing."

Doctor: "Well, maybe...then again, maybe not."

“Why reject this donor?”

- There is a risk.
- Its too risky.
- It's not safe.
- Might develop kidney disease.
- Might regret it.
- Our first duty is to the donor.
- First of all do no harm.
- Center has the right to decide appropriateness.
- Don't know what will happen after donation.

Ethics of Kidney Donor Selection

Steiner and Gert AJKD, 2000

- Centers must affirm ethical donor selection.
- All donors take risk, and risks will often vary.
- Donors must be informed, risks must be quantified.
- Donors must consent freely and rationally.
- Donor acceptance must not harm the larger transplant effort (e.g., a problem with heroes).
- Covers all issues including “boutique” issues.

How do we begin?

How do we estimate risk?

- It needs to be a risk of something over some period of time.
- It does not have to be perfect.
- Anecdotes don't count.
- Relative risks almost don't count.

“ But I HATE estimating risk!”





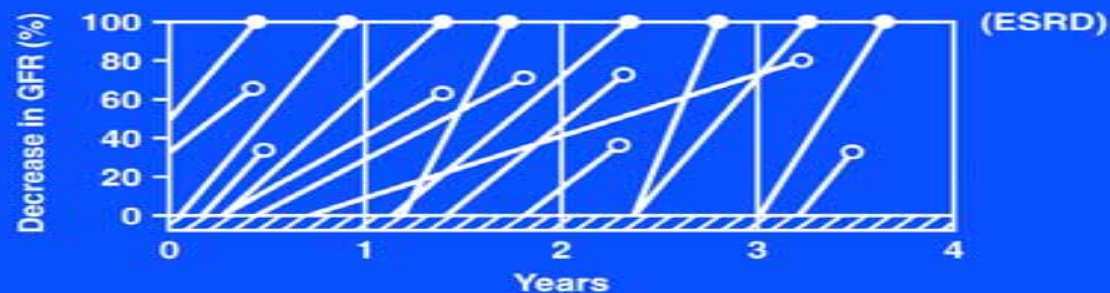
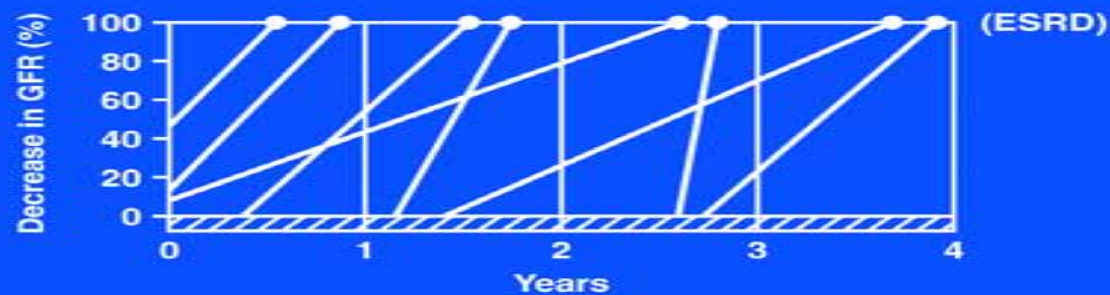
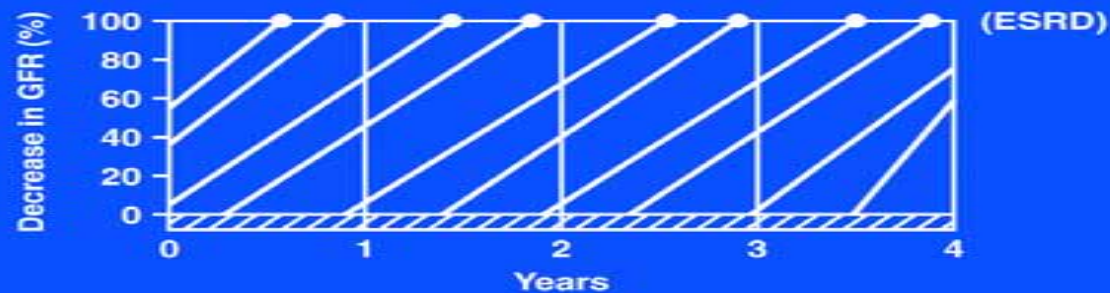
Estimating the risk for kidney failure from a blood pressure of 140/90

- At least 20% of the US population is hypertensive.
- 29,000 new cases/yr of “hypertensive ESRD”
- What is the ratio of incidence of ESRD per year to the prevalence of the risk factor?
- What is the risk of ESRD over the next 20 years?
- Are there prospective cohort study data to help us?
- Can we identify risk estimates that are erroneous?
- The 20 year risk for kidney failure is < 1 in 100 .

New ESRD 2000 => 2005 from USRDS

- Diabetes 42,000 => 47,000
- Hypertension 25,000 => 29,000
- Gomerulonephritis 8,000 => 8,000
- Cystic disease 2,000 => 2,000
- Urologic disease 1,600 => 2,000
- Other known cause 10,000 => 11,000
- Unknown cause 4,000 => 6,000
- Missing cause 4,000 => 2,000
- Total 96,000 => 107,000
- 37% at ages 45-64, 23% at ages 65-74, 26% over age 75

ESRD risk factor demographics



Why safe/unsafe donor dichotomies don't work:

- Many risk factors are a continuous extension of the normal range, e.g., BP of 125/85 vs 130/90.
- Some apparently normal young donors will develop severe renal disease over their lifetimes

Consider the young donor

- A white 18 year old has a 2-3% chance of dialysis during his life.
- A black 18 year old has a 7% lifetime risk.
- Blacks and Hispanics have a 40% lifetime chance of diabetes.
- About half the patients beginning dialysis each year are over 60.
- Risk of “normal” donors documented by recent report.

Lifetime Risk of ESRD for Unselected Non-donors

Kiberd, J Am Soc Neph, 2002

(From age 20 to 80 years)

Black woman 7.8% Black man 7.3%

White woman 1.8% White man 2.5%

By the “demographic method,” $100\text{K}/300,000\text{K}$, or $1/3,000/\text{year} \times 60$ or $60/3,000$ or 2%

Half of new ESRD each year occurs after age 65

Lifetime Risk for Diabetes Mellitus in the United States.

Narayan KMV et al, JAMA. 2003;290:1884-90.

- Diabetes was present in 7% of adults in the US in 1999, 40% increased over the preceding 10 years.
- The lifetime risk of DM for individuals born in the year 2000 is about one in three.
- White males have about a one in four lifetime risk.
- The risk in Hispanic females is highest, at over 50%.
- Diabetic risk in blacks is intermediate.

“I only want to do ‘normal’ donors! This is too complicated!”



The safe/unsafe model is an illusion.

- The normal- abnormal is a continuum.
- “Normal” donors vary as to risk by race.
- “Normal” donors are at risk in later life for hypertension, diabetes, and stones.
- “Normal” donors always sacrifice kidney function.
- The profession needs good reasons to refuse donors.

“Paternalistic” centers currently
have a leg to stand on:

- They have a duty to select donors ethically.
- The default position, when they don't know the ethics or the facts needed for a rational decision, is therefore “no.”
- Not knowing the seriousness of a particular finding is what “too risky” really means !!

Risk (and benefit) is communicated with stick figure fields, not by “high risk” and “low risk.”

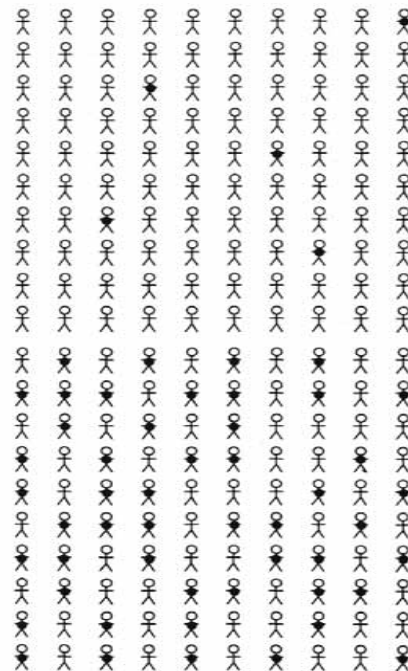
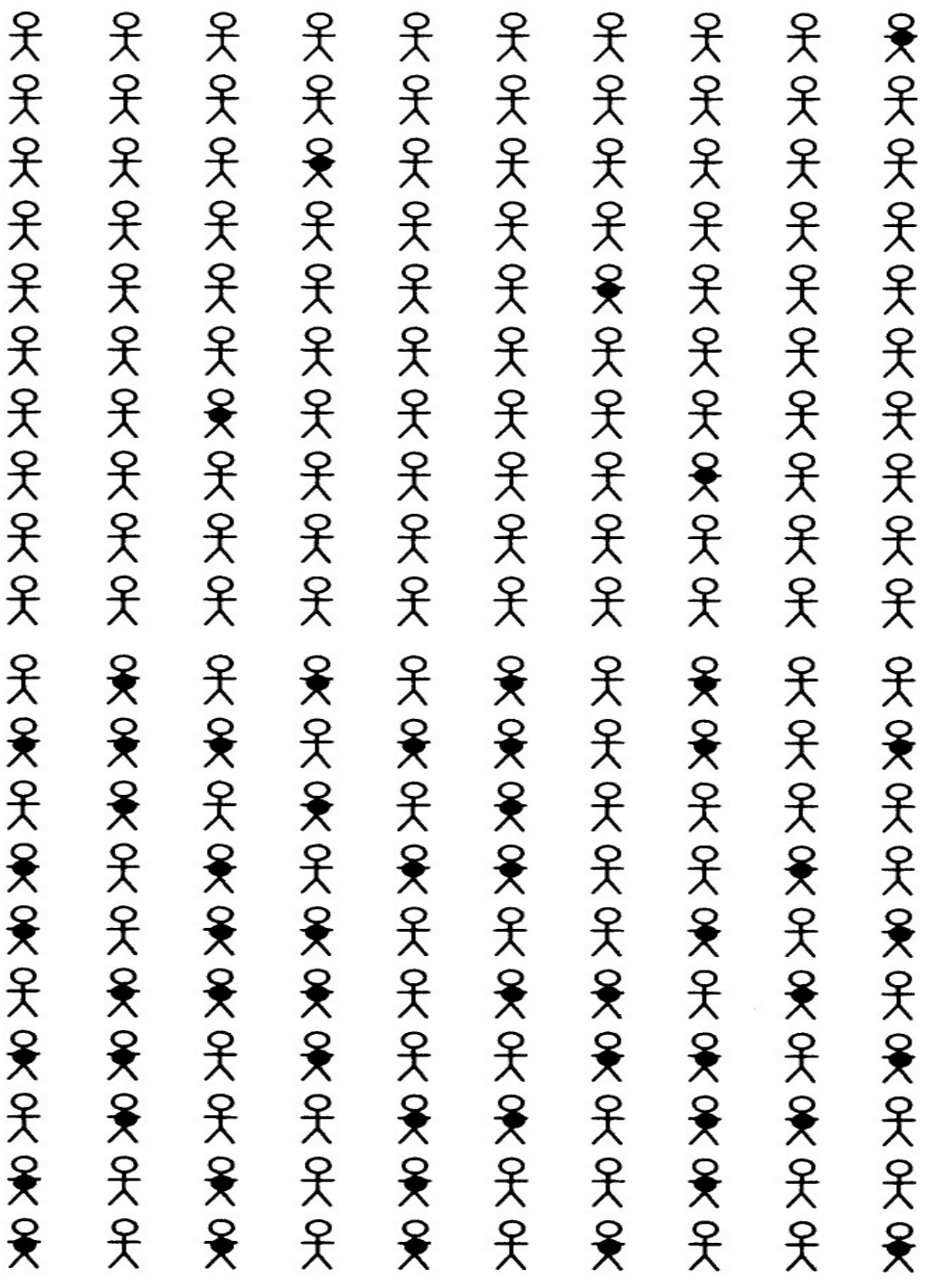


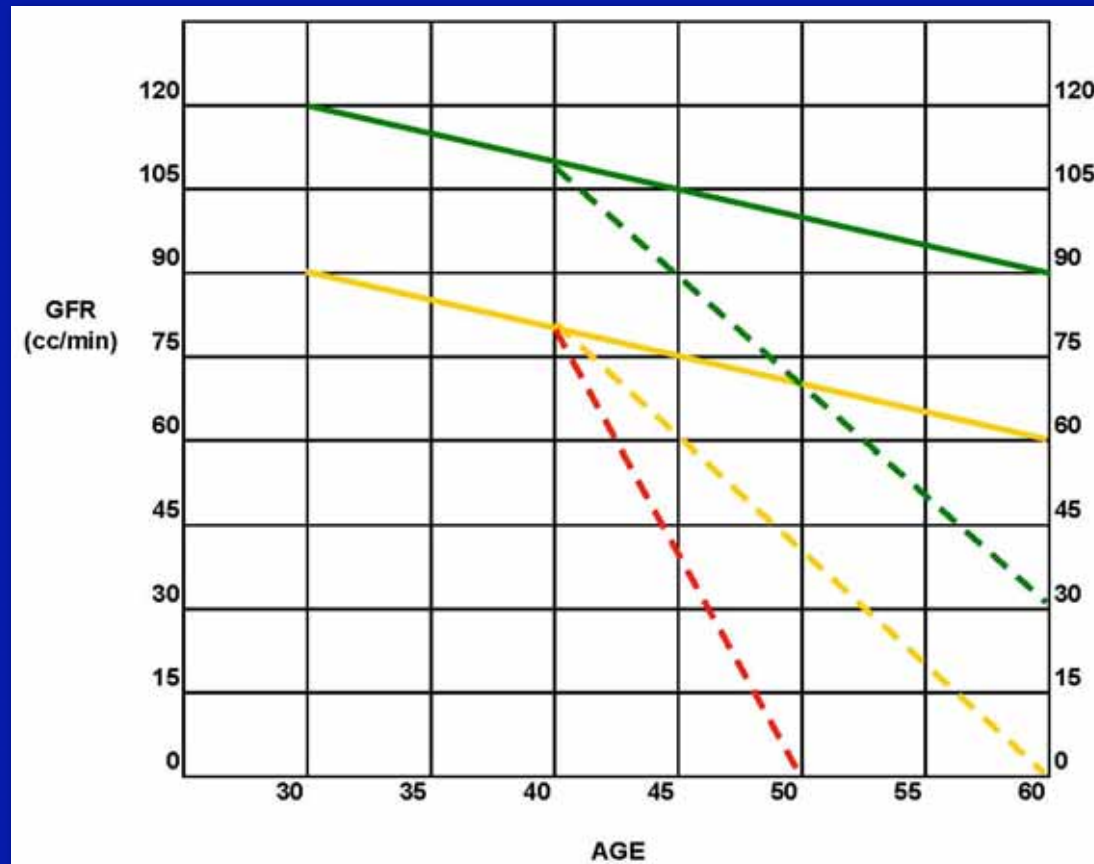
FIGURE 1. Stick figure field representative of the likelihood of allograft loss after living donor kidney transplantation. The top panel represents approximate 5% graft loss at 1 year (1). The bottom panel represents 50% graft loss at 14–15 years; because it represents one half life, it also represents graft survival over the same period (1).



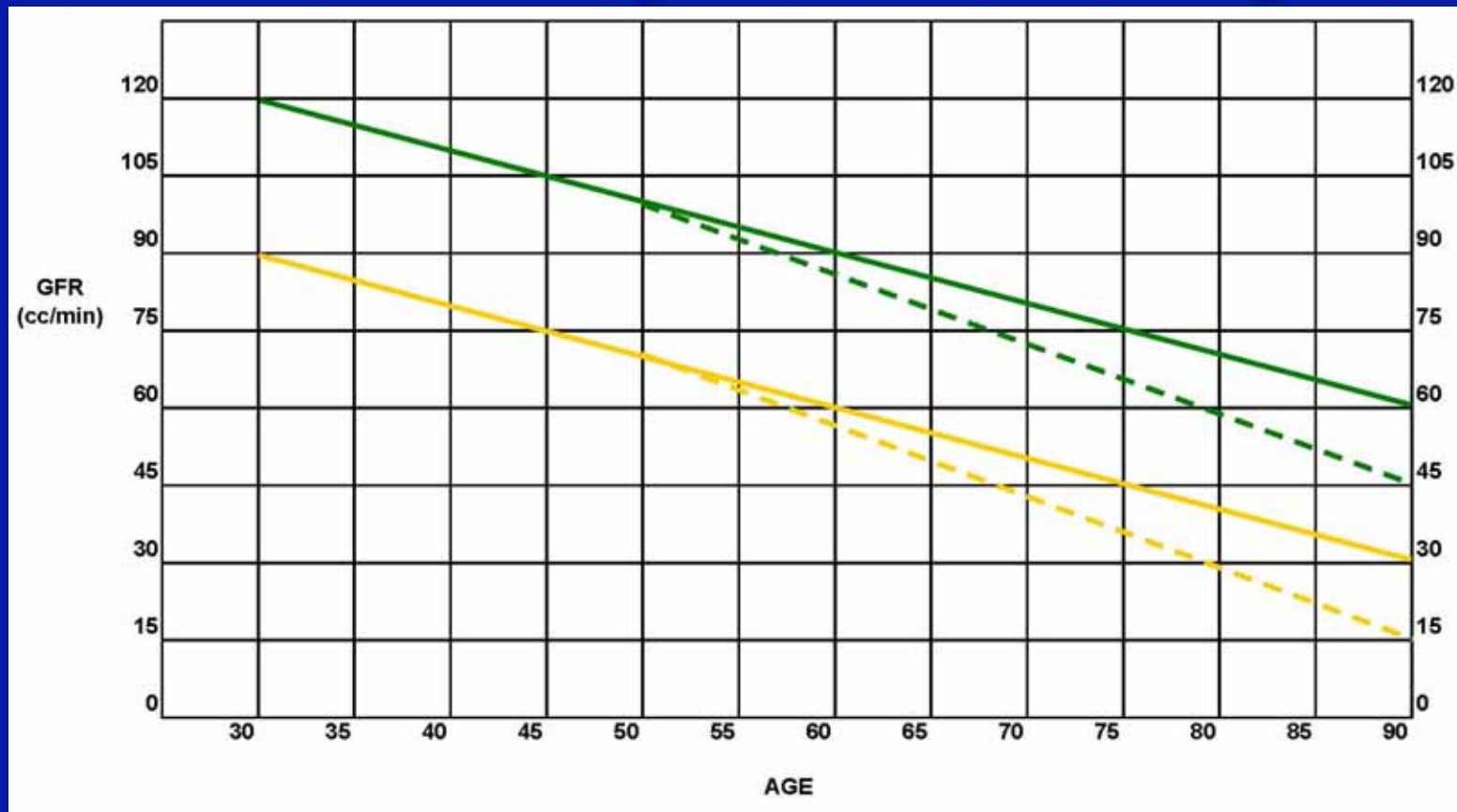
Typical True False Questions:

- If I develop a kidney problem after donation, the center will take care of me.
- Kidney transplantation is lifesaving.
- Deceased donor kidneys carry disease and probably will only work for a year or two.

What happens when progressive CKD develops after kidney donation?



Showing donors what happens when slowly progressive CKD develops 15 years after kidney donation at age 30.



To assess donors more broadly, their thinking can be formally assessed

“In making this decision, you must have decided:”

- Transplantation is better than dialysis.
- Living donor transplantation is better than deceased donor transplantation.
- I am willing to take a risk with my health.
- I can accept a bad outcome.
- I understand what I am doing.
- I do not feel pressured in any way.
- I do not need more time to think about this.

Heroes: why not let them donate?

- Heroes are informed, uncoerced, and rational and will accept greatly increased risk.
- It's not unethical to help heroes be heroic.
- But chance of “pseudo-heroism” is increased.
- Can threaten public support of transplant effort

Summary

- This effort started with reflection on what we do and what we should do in my field.
- It then required assembling of facts from previously available material.
- Finally a series of teaching and testing instruments were developed to fulfill the requirements of ethical donor selection.

But there are dangers:

- This is not a license to be “permissive” and requires more than a superficial understanding.
- It is a complicated approach that requires “reconceptualization,” work, and discipline on the part of the center.
- Many donors will still be found unacceptable.

DONE !

Ratio of new ESRD to its specific risk factor prevalence in the US

- Hypertension (20%) 60 mil / 30,000 (1/2000)
- Hematuria (2%) 6 mil / 1,500 (1/4,000)
- Nephrolithiasis (5%) 15 mil / 500 (1/30,000)
- Diabetes (5%) 15 mil / 50,000 (1/300)

“But you define two kidney risk; we need to know one kidney risk!”

- We define a risk factor by what it does in a two kidney population.
- If we want to responsibly transplant anyone at all, we had better be able to formulate the effect of removal of a kidney when kidney disease is acquired after donation.

Long term consequences of kidney donation

Ibrahim et al NEJM 2009

- 3,698 donors, age 41 +/- 11 at donation
- Mean f/u 12 +/-9 years
- GFR was 76% of pre-donation GFR
- 11 with ESRD, 22 +/- 10 years post donation

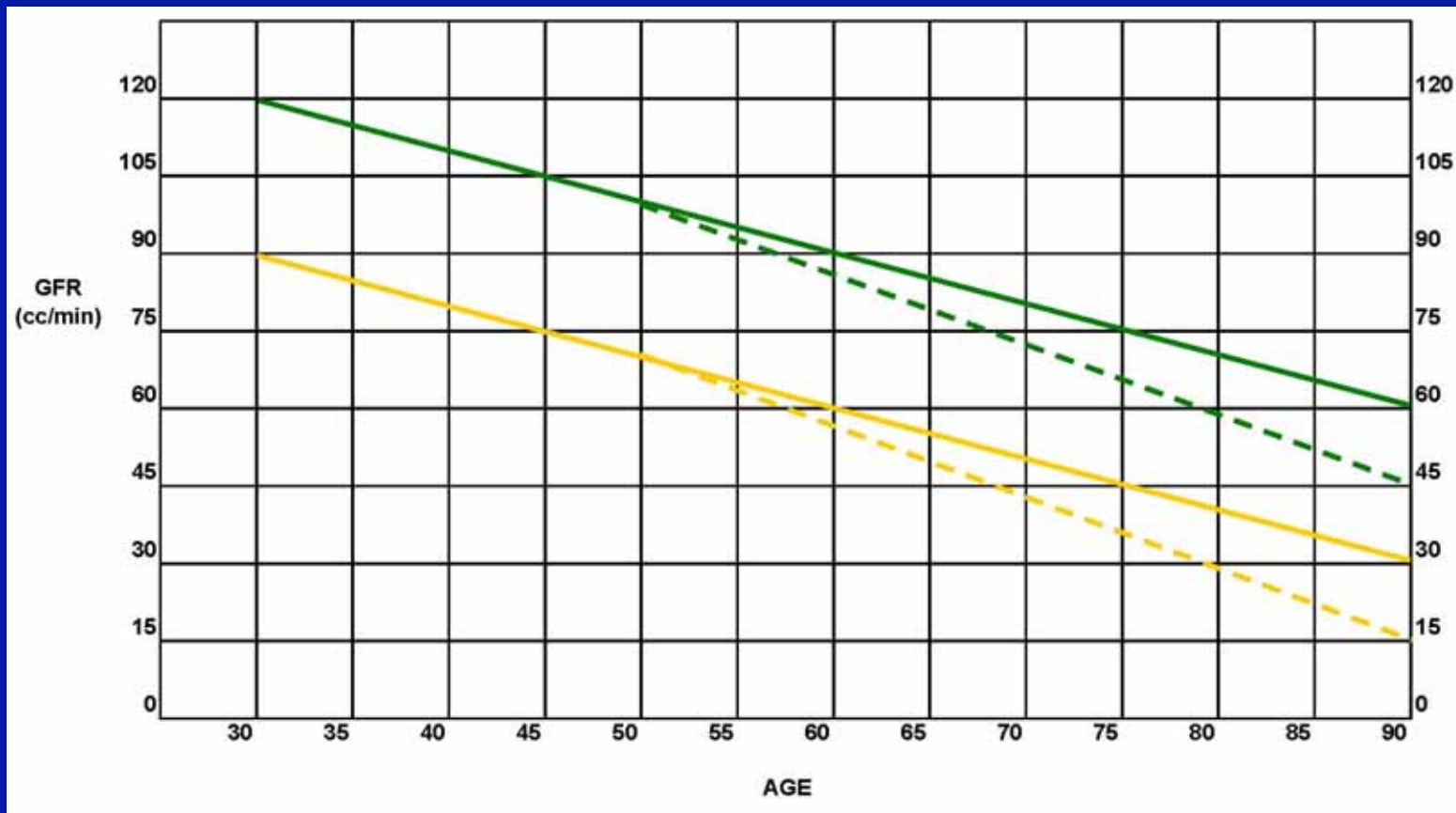
Risk vs controls was 180 vs 268/million/year, so donor risk was 2/3rds of controls.

Once risk is formulated and taught, donors are assessed by:

- True-false testing
- Stick figure fields to present risk and outcome data

Presenting the decision to donate as a involving other essential issues that a rational donor MUST address

When slowly progressive CKD develops 15 years after kidney donation at age 30.



Long term consequences of kidney donation

Ibrahim et al NEJM 2009

- 3,698 donors, age 41 +/- 11 at npx
- Mean f/u 12 +/-9 years
- GFR was 76% of pre-donation GFR
- 11 with ESRD 22 +/- 10 years after npx
- Risk vs gen'l population: 180/268/million/year

RISK OF DONORS WAS 2/3RDS OF THE GENERAL POPULATION

What does “too risky” mean in any decision making process?

- I know the risk and it is high.
- I don't know the risk at all.

There is no ethical alternative to formulating risk for all donors

- It is not reasonable for donors or centers to make important decision without researching the options and consequences.
- If these consequences cannot be formulated (and taught), donation cannot proceed.
- There will be disagreements and uncertainties, but this is not a reason not to do it.

“Defining the risk” for the donor !

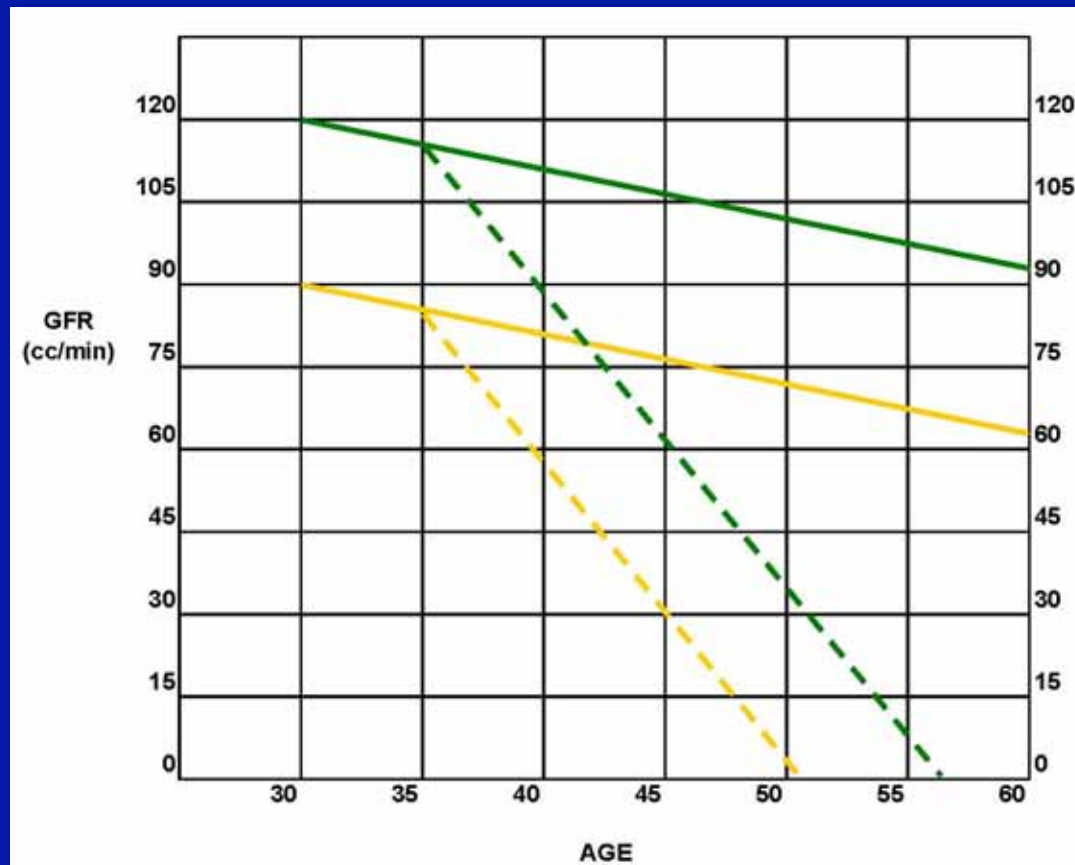
- Currently (only) lists of risks are (only) presented.
- “Low risk” or “high risk” may be added in.
- You can’t teach risk unless you know it.
- What you teach can be tested for.

Testing intuitive risk estimates for hypertensive ESRD with demographic data

- Could the 20 year risk of ESRD be 1 in 10?
- Then the one year risk is $(1/10) \times (1/20)$ or 1 in 200.
- If the prevalence of hypertension is 60 million cases,
- Each year there should be $60,000,000/200$, or 300,000 cases of hypertensive ESRD.

THIS IS NOT EVEN CLOSE!!!

When new onset, progressive CKD develops 5 years after kidney donation at age 30.



How much kidney function will I lose with donation?

- 48 studies, 3,124 patients, 1,703 controls
- 17% “immediate” loss of function
- Subsequent loss per decade about 5cc/min, less than in general population.
- Donors would therefore lose about 1/5th of the time from the onset of new renal disease to the beginning of dialysis.

(Kasiske, KI, 48:814-819,1995)

Long term consequences of kidney donation

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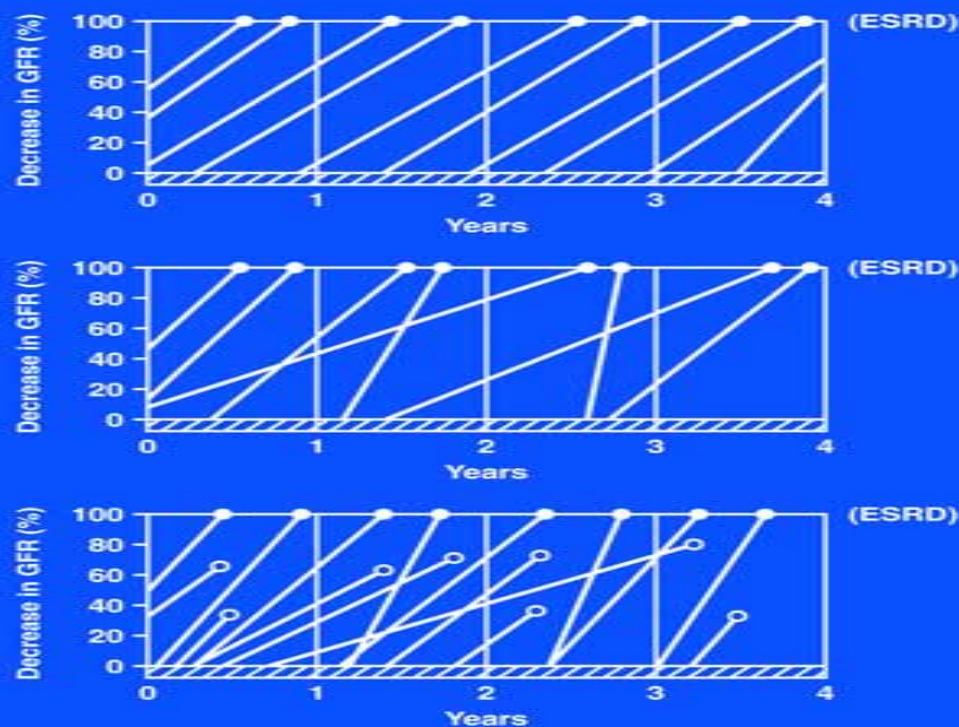
- 3,698 donors, age 41 +/- 11 at donation
- Time since donation was 12 +/- 9 years
- GFR was 76% of pre-donation GFR
- 11 with ESRD 22 +/- 10 years after donation
- Risk vs general population: 180/268/million/year (i.e., risk was 2/3rds that of the general population)

The risk of hypertensive ESRD

- 60 million U.S. adults have $BP \geq 140/90$
- 29,000/yr incidence of “hypertensive” ESRD
- Yearly risk is $< 3/6000$, 20 year risk < 1 in 100
- Includes severe and complicated hypertension.
- Represents an “upper limit” estimate.
- MRFIT trial: 3.4-4.0 ESRD/100,000 pt-yrs
- MRFIT 30 year risk 1/1000
- Meta analyses: “very little” ESRD from HBP alone

Different patterns of progression to ESRD that may arise from an at-risk fraction of a population (2 cases of ESRD per year for each pattern).

(Open circles= death before ESRD)



Areas for future discussion

- How do we address other donor abnormalities?
- How do we formulate the risk of nephrectomy?
- How do we make sure donors understand?
- How do we formally test for rational thinking?
- Is heroic donation unethical?
- What happens when we disagree?

4 reasons for refusal due to “risk”

- I do not know (have an adequate idea of) the risk.
- The risk is currently unknowable.
- I do not know how to teach you the risk.
- The risk is 1 in 10, and that's too high because ____.



True or false?

- Someone with a risk of kidney disease should not be accepted as a living kidney donor.
- Someone who might well develop or acquire a risk factor for kidney disease should not be accepted as a kidney donor?
- Someone who has a risk factor for kidney disease should not be accepted as a kidney donor?

Why estimate the risks of donation, with or without abnormal findings?

- Because we must interpret our medical findings
- Because we call risks “high” or “low.”
- Because we should responsibly accept many donors.
- Because we should responsibly exclude other donors.
- Because these risks apply to young “normal” donors.
- Because there is a continuum of risk, not “safe” and “unsafe” donors.
- Because we need to educate our donors to make defensible decisions.

Summary: Why estimate the risk of ESRD, with or without IMA's* (hypertension, stone disease, etc)?

- Because we call risks “high” or “low.”
- Because we should responsibly accept many donors.
- Because we should responsibly exclude other donors.
- Because these risks apply to young “normal” donors.
- Because there is a continuum of risk, not “safe” and “unsafe” donors.
- Because we ***always*** must educate our donors.

* IMA's = isolated medical abnormalities

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- Proteinuria (2%) 6 mil ?/ ? ?
- Diabetes (10%) 30 mil / 50,000 (1/600)

New ESRD in 2000-2005 in the US

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